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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/781,182 | 02/12/2001 | John N. Vournakis | 7867-022-999 | 2779 |

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| EXAMINER | |
|---|---|
| LEWIS, PATRICK T | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1623 | |

DATE MAILED: 04/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/781,182 | VOURNAKIS ET AL. | |
| | Examiner | Art Unit | |
| | Patrick T. Lewis | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *39-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Applicant's Response dated January 6, 2004*

1. In the Response filed November 22, 2002, claims 1-38 were canceled and claims 39-66 were added. Applicant presented arguments directed to the rejection of claims 2-17, 24-28, and 32-34 under 35 U.S.C. 103(a) as being unpatentable over Vournakis et al. US 5,635,493 (Vournakis) in view of Barton et al. *Curr. Opin. Nephrol. Hypertens.* (**1999**), vol. 8, pages 549-556 (Barton) and Pearson *Lupus* (**2000**), vol. 9, pages 183-188 (Pearson).

2. Claims 39-66 are pending. An action on the merits of claims 39-66 is contained herein below.

3. Applicant's request for reconsideration of the finality of the rejection of the Office Action dated May 6, 2003 is persuasive and, therefore, the finality of that action is withdrawn.

4. The rejection of claims 2-17, 24-28, and 32-34 under 35 U.S.C. 103(a) as being unpatentable over Vournakis et al. US 5,635,493 (Vournakis) in view of Barton et al. *Curr. Opin. Nephrol. Hypertens.* (**1999**), vol. 8, pages 549-556 (Barton) and Pearson *Lupus* (**2000**), vol. 9, pages 183-188 (Pearson) has been rendered moot in view of applicant's amendments filed January 6, 2004.

### *Response to Arguments*

5. Applicant's arguments filed January 6, 2004 have been fully considered but they are not persuasive.

Applicant argues that Vournakis does not teach the use of "non-barrier-forming" materials. In support of applicant's position, applicant has directed the examiner's attention to column 35, lines 35-48 of Vournakis.

The examiner respectfully disagrees with applicant's characterization of Vournakis. As shown in the cited passage, "p-GlcNAc based-material, such as thick gels, sponges, films and membranes may be used for such hemostatic purposes", Vournakis is not limited to "barrier-forming" compositions. Gels, sponges, films, and membranes are seen to be encompassed by the instantly invention. Applicant's attention, for example, is drawn to newly added claim 50 "wherein the non-barrier forming material is in the form of a gel, sponge, film, membrane, foam".

### *Claim Rejections - 35 USC § 112*

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 39-66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "non-barrier-forming" is critical in defining the scope of the instantly claimed invention; however, applicant has failed to particularly point out the metes and

bounds of the term. It is unclear if the barrier is permeable, semi-permeable, or non-permeable. Applicant discloses that the "non-barrier-forming" material may be in the form of a gel, sponge, film, membrane, foam, spray, emulsion, suspension, or solution, some of which are seen be a "barrier" depending on how the term is defined. Since the "non-barrier-forming" compositions have not been distinctly claimed, all claims reading on said compositions are indefinite.

### *Claim Rejections - 35 USC § 103*

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claims 39-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vournakis et al. US 5,635,493 (Vournakis) in view of Barton et al. *Curr. Opin. Nephrol. Hypertens.* (**1999**), vol. 8, pages 549-556 (Barton) and Pearson *Lupus* (**2000**), vol. 9, pages 183-188 (Pearson).

Claims 39-66 are drawn to a method for achieving at least a transient, localized, modulation of vascular structure and/or function comprising topically administering to a patient in need of said modulation, a material comprising semi-crystalline poly-β-1→4 N-acetylglucosamine polymers.

Vournakis teaches methods and compositions comprising poly-β-1→4 N-acetylglucosamine (p-GlcNAc) materials (column 36, lines 45-52). The materials may be used to promote hemostasis and wound healing (column 35, lines 40-52). The p-GlcNAc materials may be applied directly to bleeding surfaces thereby arresting bleeding by providing a mechanical matrix that promotes clotting (column 35, lines 46-48). The p-GlcNAc material comprises a crystalline polymer of high molecular weight ranging from 800,000 daltons to 30 million Daltons corresponding to a polymer having about 4,000 to about 150,000 N-acetylglucosamine monosaccharides (column 9, lines

16-25; column 13, lines 53-57). The p-GlcNAc is free of detectable protein contaminants, is substantially free of other organic contaminants such as free amino acids, and is substantially free of inorganic contaminants (column 9, lines 36-56). One or more of the monosaccharide units of the p-GlcNAc may be deacetylated with 25% to 75% remaining acetylated (column 15, lines 58-67; column 16, lines 1-8). The compositions may be in the form of mats, strings, microspheres, microbeads, membranes, fibers, powders, sponges, gels, and pharmaceutical formulations such as pills, tablets, and capsules (column 24, lines 36-44).

Vournakis differs from the instantly claimed invention in that Vournakis is silent on the compositions causing endothelin-1 release or vasoconstriction explicitly (Vournakis teaches the use of the composition for the reduction in the blood flow out of a breached vessel); Vournakis does not teach p-GlcNAc as being semi-crystalline; and Vournakis does not teach that the extent of the transient, localized modulation of vascular structure and/or function is proportional to the amount of p-GlcNAc administered. The deficiencies are, however, addressed by Pearson and Barton.

Barton teaches that the endothelin system has been implicated in the pathogenesis of arterial hypertension and renal disorders (page 549, column 1). Barton also teaches that endothelin-1 is the predominant isoform of the endothelin peptide family and regulates vasoconstriction and cell proliferation is tissues both within and outside the cardiovascular system. Pearson teaches that normal endothelial cell function is critical for all aspects of vascular homeostasis (page 183, column 1). Pearson further teaches that the active metabolism of these cells is necessary for the

continuous adjustment of vascular tone, and hence the control of blood pressure; for the physiological regulation of leukocyte traffic from blood tissues; and for the maintenance of an antithrombotic and anticoagulant balance in flowing blood (page 183, column 1).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of the prior art to arrive at the instantly claimed invention. It would have been obvious to one of ordinary skill in the art at the time of the invention that the method described by Vournakis would also induce the release of endothelin-1 and vasoconstriction since Vournakis teaches that the GlcNAc materials may be used to promote hemostasis and wound healing, and the prior art teaches that normal endothelial cell function is critical for all aspects of vascular homeostasis. It would have also been obvious to the skilled artisan that the more GlcNAc composition applied to a wound or breached blood vessel, the more bleeding would be reduced. The GlcNAc of instantly the claimed invention is described as being highly pure and semi-crystalline while the GlcNAc of Vournakis is described as being crystalline. In the absence of unexpected results, the degree of crystallinity is seen to be a measure of purity rather than a structural limitation and may thus be used interchangeably. One would have been motivated to do so in order to treat skin wounds and reduce wrinkles.

***Conclusion***

12. Claims 39-66 are pending. Claims 39-66 are rejected. No claims are allowed.

***Contacts***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on M-F 10:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patrick T. Lewis, PhD
Examiner
Art Unit 1623

James O. Wilson
Supervisory Patent Examiner
Technology Center 1600

ptl
March 29, 2004